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PATENT & TRADEMARK OFFICE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

PRUECHER et al. Group Art Unit: 1625

Serial No.: 10/069,054 Examiner: R. Covington

Filed: February 21, 2002

For: PIPERIDINE ALCOHOLS

**DECLARATION UNDER 37 C.F.R. § 1.132**

Honorable Commissionar of
Patents and Trademarks
Washington, D.C. 20231

SIR:

Gerd Bartoszyk, being duly warned, deposes and says:

I am a citizen of the Federal Republic of Germany residing at Weiterstadt, Germany;

I am a pharmacologist and biochemist by training and experience;

The degree 'Diplom-Psychologist' (at least equivalent to M.Sc.) was bestowed on me by the University of Duesseldorf, Germany; in 1982 and the degree Dr. rer. nat. by the University of Darmstadt, Germany, in 2002.

Since April 1st, 1987, I have been employed as a pharmacologist in the CNS-Department of Merck KGaA, Darmstadt, Germany;

I am author or co-author of numerous papers and patents in the fields of pharmacology, biochemistry and the development of drugs.

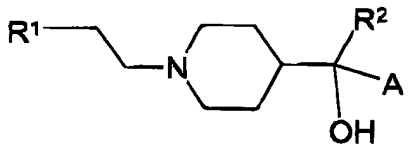
Furthermore, I am familiar with the present application Ser. No. 10/069,054.

I have carried out, or supervised experiments for testing 5-$HT_{2A}$ antagonistic properties according to the methods described within the genus claimed in the pending application.

In comparison to a compound of the prior art a representative compound of present application exhibits an unexpected improved suppression of the behaviour induced by DOI.

## Pharmacological Report

Suppression of behaviour elicited (head-twitching in mice) by a representative compound of the formula I (DOI antagonism)




I

A = $CH_3$ (if not stated otherwise)

in comparison to a compound cited in EP 0531410 (WO 91/18602).

| $R^1$ | $R^2$ | Salt | Racemate (rac)/ Enantiomer (+) oder (-) | M.p.. [°C] | Inhibition [%] |
|---|---|---|---|---|---|
| 4-Fluorphenyl | 2,3-Dimethoxy-phenyl | HI | rac | 199-200 | 71 |
| | | | | | |
| Comparison from EP 0531410: | | | | | |
| 4-Fluorphenyl*** | 2,3-Dimethoxy-phenyl | | | | 0 |

*** A = H

The compound of the formula I according to the invention inhibits the head twitching induced in mice by DOI by 71 % at an oral dose of 1 mg/kg (71 % antagonism).

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

January 24, 2003
Date

Gerd Bartoszyk

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(54) Title: (+)-α-(2,3-DIMETHOXYPHENYL)-1-[2-(4-FLUOROPHENYL)ETHYL]-4-PIPERIDINEMETHANOL

(57) Abstract

The present invention is directed to a new $5HT_2$ antagonist, (+)-α-(2,3-dimethoxyphenyl)-1-[2-(4-fluorophenyl)ethyl]-4-piperidinemethanol, and its use in the treatment of a number of disease states.